

### **REMARKS/ARGUMENTS**

#### **The Application Complies with the Sequence Rules**

The Office Action indicates on page 2 that the application does not comply with the sequence rules because "[s]equence identifiers are missing from the sequences in ¶3 on page 32, ¶1 on page 33, ¶1 on page 36, ¶2 on page 39, ¶2 on page 42, ¶2 on page 2, and ¶2 on page 44."

Applicant respectfully disagrees with this position of the Office because he previously amended the specification to insert sequence identifiers into each of these paragraphs by way of the Preliminary Amendment filed June 2, 2006, with one exception. Applicant did not amend ¶2 on page 2, because this paragraph does not contain any nucleotide and/or amino acid sequences. Possibly, the Examiner intended to refer to ¶2 on page 43, which contains nucleotide and/or amino acid sequences. Applicant amended ¶2 on page 43 to include the required sequence identifiers by way of the Preliminary Amendment filed June 2, 2006.

Should the Examiner be unable to locate the Preliminary Amendment filed June 2, 2006, Applicant will upon request supply the Examiner with a copy. Applicant notes, however, that as of the date of the instant Amendment, the Preliminary Amendment filed June 2, 2006 can be found in the Patent Application Information Retrieval (PAIR) record for the instant application.

In view of the Preliminary Amendment filed June 2, 2006, Applicant submits that the application complies with the sequence rules.

#### **Request for Confirmation that the Amended Claims Are Under Examination**

Applicant respectfully requests that the Examiner confirm in the next Office Action that the claims she examined for the instant Office Action are the claims as amended in the Preliminary Amendment filed June 2, 2006. Given the Examiner's failure to consider the amendments to the specification presented in the Preliminary Amendment filed June 2, 2006,

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Applicant is concerned that the Examiner might not have considered the claims as amended in the Preliminary Amendment.

If the Examiner has not yet considered the claims as amended in the Preliminary Amendment filed June 2, 2006, Applicant respectfully requests the Examiner to withdraw the instant Office Action, consider the claims as amended in the Preliminary Amendment, and issue a new, non-final Office Action.

#### Status of the Claims

Claims 1-28 and 30-42 stand rejected, and claim 29 has been withdrawn.

Applicant has amended claims 1, 36, 41, and 42.

Applicant has amended claim 1 to recite that the control signal is selected from the group consisting of lactose or an analog of lactose and that the plant or plant cells contain in the plastid genome a recombinant nucleic acid comprising said sequence of interest and, operably linked thereto, a lac operator, said plant or said plant cells further having or encoding an intra-plastid lac repressor.

Applicant has amended claim 36 to recite that the plant or plant cells comprise in the plastid genome a recombinant nucleic acid comprising said sequence of interest operably linked to a lac operator, said plant or said plant cells further having or encoding an intra-plastid lac repressor.

Applicant has amended claim 41 to recite that the sequence of interest is operably linked to a lac operator and with a heterologous nucleotide sequence encoding an intra-plastid lac repressor.

Applicant has amended claim 42 to recite that the control signal is lactose or an analog of lactose. Applicant has also amended claim 42 to independent form by incorporating the limitations of amended claim 36. As amended, the claim recites that the system comprises (a) a

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plant or plant cells capable of controlled expression of a plastome-encoded sequence of interest, said plant or plant cells comprising in the plastid genome a recombinant nucleic acid comprising said sequence of interest operably linked to a lac operator, said plant or said plant cells further having or encoding an intra-plastid lac repressor, and (b) lactose or an analog of lactose for controlling expression of said sequence of interest in said plant or plant cells.

Support for the amendment to claims 1, 36, 41, and 42 can be found in original claims 1, 5, 7, 36, 40, 41, and 42, and in the specification, particularly on pages 8, 11, 12, 14, 21, 24, 26, and 30.

Applicant has cancelled claims 2-25, 29-35, and 37-40 without prejudice or disclaimer. Applicant has cancelled claim 29 because this claim is directed to non-elected subject matter.

Applicant expressly reserves the right to file continuing applications or take such other appropriate measures deemed necessary to protect the full scope of the subject matter that is encompassed by the original claims.

New claims 43-47 have been added. Support for the new claims can be found in original claims 5 and 7, and in the specification, particularly on pages 6-12, 19- 21, and 30

No new matter has been added by way of amendment of the claims or by the addition of the new claims.

Claims 1, 26-28, 36, and 41-47 are pending.

Reexamination and reconsideration of the application as amended are respectfully requested in view of the following remarks.

The Rejections of the Claims Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1-2, 6, 20, 22-28, and 30-42 have been rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. Claims 2, 6, 20, 22-

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25, 30-35, and 37-40 have been cancelled. Claims 1, 36, 41, and 42 have been amended. New claims 43-47 have been added. This rejection is respectfully traversed and should not be applied to the newly added claims.

The Office Action indicates that the claims require nucleic acids that encode translation regulatory RNAs but that the only translation regulatory RNAs described in the specification are RNA aptamers. The Office Action alleges that the specification fails to describe the structural features of any translation regulatory RNAs that are not RNA aptamers. The Office Action further alleges that because these nucleic acids are not described, methods of using them are not described. The Office Action concludes that the specification fails to provide an adequate written description of the claimed invention.

Without conceding to this position of the Office Action, Applicant has amended claims 1, 36, 41, and 42 in the interest of expediting prosecution of the instant application and not to limit the scope of his claimed invention. As amended, these four independent claims and their respective dependent claims (including new claims 43-47) are not directed to nucleic acids that encode translation regulatory RNAs. Therefore, the rejection of the claims for failing to comply with the written description requirement has been overcome.

In view of the amendments and remarks, it is submitted that the rejections under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement should be withdrawn and not applied to the newly added claims.

The Rejections of the Claims Under 35 U.S.C. § 112, Second Paragraph, Is Moot

Claims 6, 9, and 16 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 6, 9, and 16 have been cancelled. New claims 43-47 have been added. This rejection is now moot due to the cancellation of claims 6, 9, and 16 and should not be applied to the newly added claims.

The Office Action alleges that claims 6, 9, and 16 are indefinite because each of these claims recites a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation.

Applicant has cancelled claims 6, 9, and 16 making this rejection moot. Furthermore, new claims 43-47 are not susceptible to rejection because none of the new claims recites a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation. Accordingly, this rejection should not be applied to the newly added claims.

The Rejections of the Claims Under 35 U.S.C. § 102(b) Should Be Withdrawn

Claims 1-6, 9-13, 15-19, 26, 28, 30-39, 41, and 42 have been rejected under 35 U.S.C. § 102(b). Claims 1, 2, 6, 9-13, 15-18, 26, 30, 32-34, 36, and 37 have been rejected as being anticipated by McBride *et al.* (1999, U.S. Patent No. 5,925,806). Claims 1-6, 9-11, 19, 26, 28, 30, 31, 33-39, 41, and 42 have been rejected as being anticipated by McBride *et al.* (WO 01/02593). Claims 2-6, 9-13, 15-19, 30-35, and 37-39 have been cancelled. Claims 1, 36, 41, and 42 have been amended. New claims 43-47 have been added. These rejections are respectfully traversed and should not be applied to the newly added claims.

The Examiner alleges that the McBride *et al.* patent (U.S. Patent No. 5,925,806) discloses all of the limitations of each of claims 1, 2, 6, 9-13, 15-18, 26, 30, 32-34, 36, and 37. The Office Action further alleges that the McBride *et al.* application (WO 01/02593) discloses all of the limitations of each of claims 1-6, 9-11, 19, 26, 28, 30, 31, 33-39, 41, and 42.

Applicant respectfully acknowledges that the Examiner has determined that that claims 7 or 40 are not anticipated by either the McBride *et al.* patent or the McBride *et al.* application.

Without conceding to the position of the Office Action that the McBride *et al.* patent and the McBride *et al.* application anticipate Applicant's claimed invention, Applicant has amended claims 1, 36, 41, and 42 in the interest of expediting prosecution of the instant application and not to limit the scope of his claimed invention. As amended, claim 1 includes the limitations of

claim 7. Likewise, amended claims 36, 41, and 42 have been amended to include similar limitations as amended claim 1 such that these claims are now drawn to a plant or plant cells or producing a plant or plant cells that comprise a lac operator and that have or encode an intra-plastid lac repressor. Furthermore, new claims 43-47, which depend from either amended claim 1, 36, or 42, also include these limitations. Accordingly, neither the McBride *et al.* patent nor the McBride *et al.* application anticipates the amended claims and the newly added claims.

In view of the amendments and remarks, it is submitted that the rejection of the claims under 35 U.S.C. § 102(b) should be withdrawn and should not be applied to newly added claims.

The Rejections of the Claims Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 1-28 and 30-42 have been rejected under 35 U.S.C. § 103(a). Claims 1-11, 17-19, 26-28, 30-31, and 33-42 have been rejected as being unpatentable over McBride *et al.* (WO 01/02593) in view of Maliga (1996, U.S. Patent No. 5,530,191). Claims 1-6, 9-11, 19-26, 28, 30-31, 33-39, 41, and 42 have been rejected as being unpatentable over McBride *et al.* (WO 01/02593) in view of Suess *et al.* (2004, Nuc. Acids Res. 32:1610-1614). Claims 1-2, 6, 9-18, 26, 30, 32-34, 36, and 37 have been rejected as being unpatentable over McBride *et al.* (1999, U.S. Patent No. 5,925,806). Claims 1, 36, 41, and 42 have been amended. Claims 2-25, 30-35, and 37-40 have been cancelled. New claims 43-47 have been added. This rejection is respectfully traversed and should not be applied to the newly submitted claims.

Applicant respectfully acknowledges that the Examiner has determined that claims 7 and 40 are not obvious in view of either the combination of McBride *et al.* (WO 01/02593) and Suess *et al.* or the McBride *et al.* patent (U.S. Patent No. 5,925,806).

As discussed above, Applicant has amended claims 1, 36, 41, and 42 in the interest of expediting prosecution of the instant application. As amended, claim 1 includes the limitations of claim 7. Likewise, amended claims 36, 41, and 42 have been amended to include similar limitations as amended claim 1 such that these claims are now drawn to a plant or plant cells or

producing a plant or plant cells that comprise a lac operator and that have or encode an intra-plastid lac repressor. Furthermore, new claims 43-47, which depend from either amended claim 1, 36, or 42, also include these limitations. Given that the claims are now directed to processes, plants, plant cells, or systems that relate to a plant or plant cells, or the making of plant or plant cells, that comprise a lac operator and that have or encode an intra-plastid lac repressor, Applicant submits that amended claims are not obvious in view of either the combination of McBride *et al.* (WO 01/02593) and Suess *et al.* or the McBride *et al.* patent.

Applicant respectfully disagrees with the position of the Office Action that claims 1-11, 17-19, 26-28, 30-31, and 33-42 are unpatentable over the McBride *et al.* application (WO 01/02593) in view of Maliga (1996, U.S. Patent No. 5,530,191) for the reasons that are discussed below.

The McBride *et al.* application relates *inter alia* to a process of controlling nuclear and plastid gene expression of a eukaryotic cell using the AHL quorum sensing system.

The McBride *et al.* application contains some disclosure on controlling nuclear gene expression of a eukaryotic cell. Little disclosure on controlling plastid gene expression of a eukaryotic cell is provided, however. Notably, no example demonstrating functionality in plastids is present in the McBride *et al.* application. The section from the third paragraph on page 43 to page 45, top, describes certain constructs, but no process of controlling expression of a plastome-encoded sequence of interest, comprising externally applying to a plant or to plant cells a chemical control signal. Further, use of the present tense indicates that these constructs have not been prepared, whereby no experimental tests using these constructs could have been carried out.

Paragraphs 1 to 3 on page 50 ("Transplastomic Plant Analysis") report an experiment wherein transcription of the GUS transgene is dependent on the application of AHL. However, no information is provided on what the plastid-transformed plants were transformed with. According to Example 4, Section 4B "Plastid Transformation" (page 45-46), plastids were

transformed with plasmids pZS223 and pZS224. However, these plasmids are not described in this document. Thus, the skilled person does not know what was transformed into plant plastids in the experiment reported on page 50. It is unlikely that the constructs described on pages 43-45 were transformed into plant plastids, since they apparently have not been actually produced.

In summary, the McBride *et al.* application can at best be considered a suggestion for a research project on creating a process for controlling expression of a plastome-encoded sequence of interest.

The invention as presently claimed differs from the McBride application in that the McBride application does not describe a process of controlling expression of a plastome-encoded sequence of interest in a plant or in plant cells by externally applying to said plant or to said plant cells a control signal selected from lactose or an analog of lactose, wherein said plant or said plant cells contain in the plastid genome a recombinant nucleic acid comprising said sequence of interest and, operably linked thereto, a lac operator, said plant or said plant cells further having or encoding an intra-plastid lac repressor.

Maliga (US 5,530,191) does not relate to a process of controlling expression of a plastome-encoded sequence of interest by externally applying to a plant or to plant cells a chemical control signal. Instead, Maliga relates to a cytoplasmic male sterility (CMS) system for plants. CMS systems are used for producing hybrid seeds of agronomically important plants. In CMS systems such as the one disclosed in Maliga, expression of a gene involved in CMS is controlled by crossing of parental plants. No lactose or lactose analog is used in the CMS systems of Maliga.

More specifically, in Maliga (column 13, first and second full paragraph) a lac repressor encoded by a restorer line of CMS is crossed with a male-sterile plant for producing hybrid male-fertile seed. The male-sterile plant contains in plastids a plastid-toxic killer gene operably linked to a T7/lac promoter. Upon crossing of the male-sterile plant with the restorer line, plastid-targeted lac repressor is expressed and binds to the lac promoter, thereby preventing transcription



of the plastid-toxic killer gene. Thus, Maliga controls gene expression by crossing plants, instead of by externally applied lactose or an analog thereof. Therefore, Maliga is so remote from the system of the McBride application that the skilled person knowing the McBride application has no reason to consider Maliga.

Even if the skilled person knew, by chance, Maliga, the skilled person cannot arrive at the invention as presently claimed for the following reasons.

1. Neither the McBride application nor Maliga suggest that lactose or an analog thereof can be used for controlling expression of a plastome-encoded sequence of interest in a plant or in plant cells. Notably, there is no indication in the prior art that lactose or a lactose analog can cross the two-membrane envelope of plastids. In plastids, entry and exit of molecules is regulated, and there is no known transport system for lactose over the plastid two-membrane envelope. Further, lactose or the analog thereof has to cross the plant cell plasma membrane as well as the cell wall to even have the possibility of entering into plastids. It is therefore surprising that the lac system can be used for controlling gene expression of a plastome-encoded sequence of interest in plants or plant cells.
2. A combination of the lac repressor as used by Maliga with externally applied lactose or an analog thereof is excluded by the fact that the presence of lactose would prevent the desired repressive effect caused by the lac repressor.
3. The Examiner, with reference to page 18, ¶2 of the McBride application is of the opinion that the McBride application teaches that the tetR system is analogous to the luxR system. The cited text portion relates to a two-factor system for achieving "active" repression of transcription. No suggestion can be derived from the cited text portion that the tet system can be used for controlling expression of a plastome-encoded sequence of interest. No

suggestion is found that tetracycline could cross the double-membrane envelope of plastids for interacting with an intra-plastid component of the plastid protein expression machinery. Importantly, no information is found that the tet two-factor system should be analogous to the lac system. Importantly, the chemical structures of tetracycline and lactose or analogs thereof are unrelated, so that the tet system and the lac system are clearly non-analogous. Even if the prior art suggested that tetracycline could cross the plastid two-membrane envelope, no conclusions could be drawn from such suggestion to the ability of lactose to cross the plastid two-membrane envelope. This shows that the type of operator system is clearly not a design choice for controlling expression of a plastome-encoded sequence of interest.

In summary, one of skill in the art would not find that the subject matter encompassed by the amended claims is obvious in view of the combination of the McBride *et al.* application and Maliga. As discussed above, one of skill in the art would not have combined McBride *et al.* application and Maliga to make Applicant's invention as presently claimed. More importantly, even if the skilled person had combined the McBride *et al.* application with Maliga, this combination fails to provide all of the elements of the amended claims. Therefore, the Examiner has failed to raise a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

Furthermore, one of skill in the art would not find that the subject matter encompassed by the new claims is obvious in view of the combination of the McBride *et al.* application and Maliga for the same reasons as stated above because the new claims are within the scope of either amended claim 1, 36, or 42.

In view of the amendments and remarks, it is submitted that the rejection of claims under 35 U.S.C. § 103(a) should be withdrawn and should not be applied to the newly added claims.

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## **CONCLUSION**

In view of the above amendments and remarks, Applicant submits that the rejections of the claims under 35 U.S.C. §§ 102, 103, and 112 are overcome. Applicant respectfully submits that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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